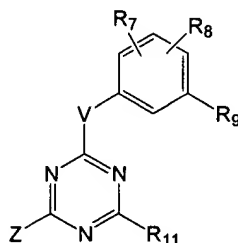


**CLAIM AMENDMENTS**

Below is a complete listing of all claims and replaces all prior versions.

1-65. (Canceled).

66 (Previously presented). A compound of Formula (I),



**I**

or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt, or solvate thereof, wherein:

V is chosen from  $-\text{CHR}^5-$ ,  $-\text{NR}^5-$ ,  $-\text{O}-$ , and  $-\text{S}-$ ;

Z is chosen from halogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl,  $-\text{SR}^3$ ,  $-\text{OR}^3$ , and  $-\text{N}(\text{R}^1)(\text{R}^2)$ ;  $-\text{N}(\text{R}^1)(\text{R}^2)$  taken together may form a heterocyclyl or substituted heterocyclyl; or

R<sup>1</sup> is chosen from hydrogen, alkyl and substituted alkyl; and

R<sup>2</sup> is chosen from alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R<sup>3</sup> is chosen from hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R<sup>5</sup> is chosen from hydrogen and alkyl, or when attached to a nitrogen atom, R<sup>5</sup> taken together with R<sup>7</sup> may form a fused heterocyclyl or substituted heterocyclyl;

R<sup>7</sup> is chosen from hydrogen,  $-\text{N}(\text{R}^{31})(\text{R}^{32})$ , halogen, cyano, alkyl, substituted alkyl, alkoxy, and alkylthio, or when V is  $-\text{NR}^5$ ,  $-\text{R}^5$  and R<sup>7</sup> taken together may form a fused heterocyclyl or substituted heterocyclyl;

R<sup>8</sup> is chosen from hydrogen and halogen;

R<sup>9</sup> is chosen from  $-\text{CO}_2(\text{alkyl})$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{SO}_2\text{N}(\text{R}^{31})(\text{R}^{32})$ ,

$-N(R^{33})SO_2R^{34}$ ,  $-C(O)N(R^{33})N(R^{31})(R^{32})$ ,  $-N(R^{33})C(O)R^{34}$ ,  $-CH_2N(R^{33})C(O)R^{34}$ ,  $-N(R^{31})(R^{32})$ ,  $-CH_2OC(O)R^{34}$ ,  $C_{1-6}$ alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclyl, substituted heterocyclyl, and  $-C(O)R^{10}$ ; provided, however, that when  $R^9$  is  $CH_3$  or  $NH_2$ , then neither  $R^2$  nor  $R^{14}$  is *para*-cyano-phenyl;

or  $R^8$  and  $R^9$  taken together may form  $-C(O)N(R^{33})CH_2-$  or  $-C(O)N(R^{33})C(O)-$ ;

$R^{10}$  is chosen from heterocyclyl, substituted heterocyclyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkyl, and substituted alkyl;

$R^{31}$  and  $R^{33}$  are independently chosen from hydrogen, alkyl, and substituted alkyl;

$R^{32}$  is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, aryloxy, heterocyclyl and substituted heterocyclyl;

$R^{34}$  is chosen from alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

$R^{11}$  is  $-N(R^{12})(R^{13})$ ;

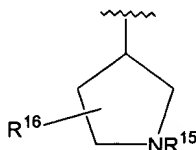
$R^{12}$  is chosen from hydrogen, alkyl, and substituted alkyl; and

$R^{13}$  is  $-(CH_2)_mR^{14}$ ; or

$-N(R^{12})(R^{13})$  taken together may form a heterocyclyl or substituted heterocyclyl;

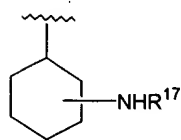
$m$  is 0, 1, 2 or 3;

$R^{14}$  is chosen from alkyl, substituted alkyl,  $-C(O)N(R^{31})(R^{32})$ ,  $-N(R^{33})C(O)R^{34}$ , aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, and



$R^{15}$  is chosen from hydrogen, alkyl, substituted alkyl, alkenyl,  $-C(O)$ -alkyl,  $-C(O)$ -substituted alkyl,  $-C(O)$ -aryl,  $-C(O)$ -substituted aryl,  $-C(O)$ -alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

$R^{16}$  is chosen hydrogen, alkyl, substituted alkyl, and

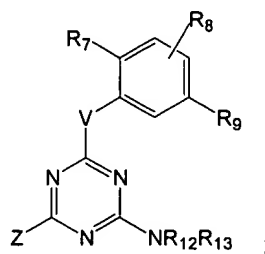


or

$R^{17}$  is chosen from hydrogen, alkyl, substituted alkyl,  $-C(O)$ -alkyl,  $-C(O)$ -substituted alkyl,  $-C(O)$ -aryl, and  $-C(O)$ -substituted aryl.

67-69 (Canceled).

70. (Previously presented). A compound having the formula,



or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt, or solvate thereof, wherein:

V is chosen from  $-CHR^5-$ ,  $-NR^5-$ ,  $-O-$ , and  $-S-$ ;

Z is halogen, alkyl,  $-N(R^1)(R^2)$ , or alkyl substituted with one to two of  $-N(R^{31})(R^{32})$ , alkoxy, alkylthio, halogen, cyano, carboxyl, hydroxyl,  $-SO_2$ -alkyl,  $-CO_2$ -alkyl,  $-C(O)$ -alkyl, nitro, cycloalkyl, substituted cycloalkyl,  $-C(O)-N(R^{31})(R^{32})$ , and/or  $-NH-C(O)$ -alkyl;

$R^1$  is hydrogen or methyl;

$R^2$  is alkyl of 1 to 8 carbon atoms;

$R^3$  is chosen from hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

$R^5$  is chosen from hydrogen and alkyl of 1 to 4 carbon atoms;

$R^7$  is chosen from hydrogen, amino, amino $C_{1-4}$ alkyl, halogen, cyano,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkoxy, and alkylthio;

$R^8$  is attached to any available carbon atom of the phenyl ring and is chosen from hydrogen and halogen;

$R^9$  is chosen from  $-C(O)N(R^{31})(R^{32})$ ,  $-SO_2N(R^{31})(R^{32})$ ,  
 $-N(R^{33})SO_2R^{34}$ ,  $-C(O)N(R^{33})N(R^{31})(R^{32})$ ,  $-N(R^{33})C(O)R^{34}$ ,  $-CH_2N(R^{33})C(O)R^{34}$ ,  
 $-N(R^{31})(R^{32})$ ,  $-CH_2OC(O)R^{34}$ , heterocyclyl, and substituted heterocyclyl; or

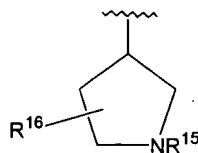
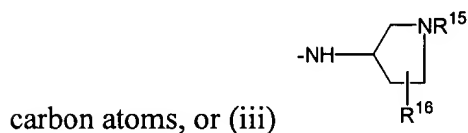
$R^8$  and  $R^9$  taken together may form  $-C(O)N(R^{33})CH_2-$  or  $-C(O)N(R^{33})C(O)-$ ;

$R^{31}$  and  $R^{33}$  are independently chosen from hydrogen, alkyl, and substituted alkyl;

$R^{32}$  is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl,  
cycloalkyl, substituted cycloalkyl, aryloxy, heterocyclyl and substituted heterocyclyl;

$R^{34}$  is chosen from alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted  
cycloalkyl, heterocyclyl and substituted heterocyclyl;

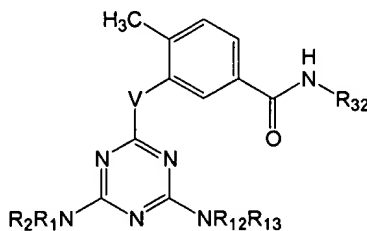
$-N(R^{12})(R^{13})$  taken together form (i) a monocyclic heterocyclyl or substituted heterocyclyl of  
5 to 7 atoms having 1, 2 or 3 additional nitrogen atoms, (ii)  $-NH$ -alkyl wherein alkyl is of 1 to 4



$R^{15}$  and  $R^{16}$  are independently hydrogen or methyl; and

$R^{17}$  is chosen from hydrogen, alkyl, substituted alkyl,  $-C(O)$ -alkyl,  
 $-C(O)$ -substituted alkyl,  $-C(O)$ -aryl, and  $-C(O)$ -substituted aryl.

71 (Previously presented). A compound of Claim 70 or a enantiomer, diastereomer,  
tautomer, or pharmaceutically-acceptable salt, or solvate thereof, having the formula:



72 (Previously presented). The compound of claim 70 or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt or solvate thereof, wherein:

$R^7$  is halogen, methyl, methoxy, halogen, or cyano.

73 (Previously presented). The compound of claim 70 or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt or solvate thereof, wherein:

$R^9$  is  $C(=O)NH_2$ ,  $C(=O)NH(CH_3)$ , or  $C(=O)NHO(CH_3)$ .

74 (Previously presented). The compound of claim 70 or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt, or solvate thereof,

wherein  $R^7$  is methyl and  $R^9$  is  $C(=O)NH(CH_3)$  or  $C(=O)NHO(CH_3)$ .

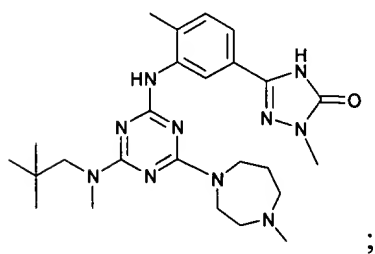
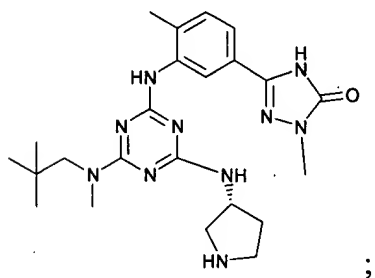
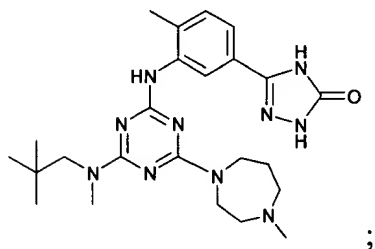
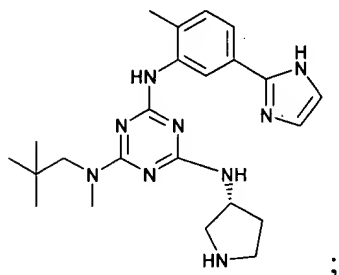
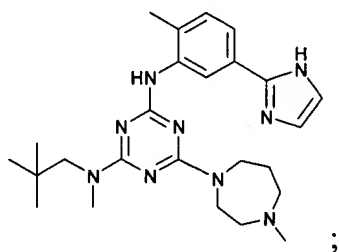
75 (Previously presented). A compound of Claim 70 or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt or solvate thereof wherein:

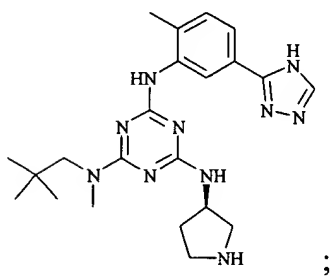
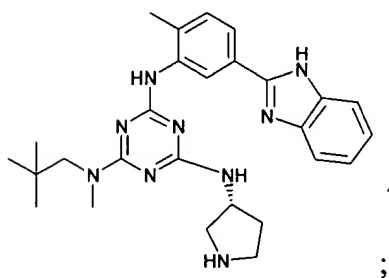
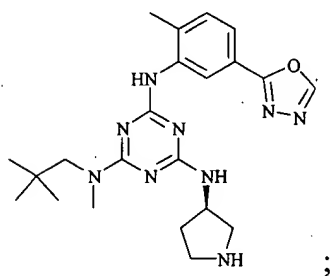
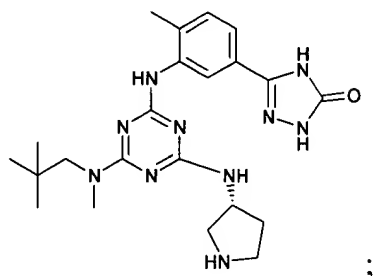
$R^9$  is chosen from unsubstituted or substituted triazolyl, oxadiazolyl, imidazolyl, thiazolyl and benzimidazolyl.

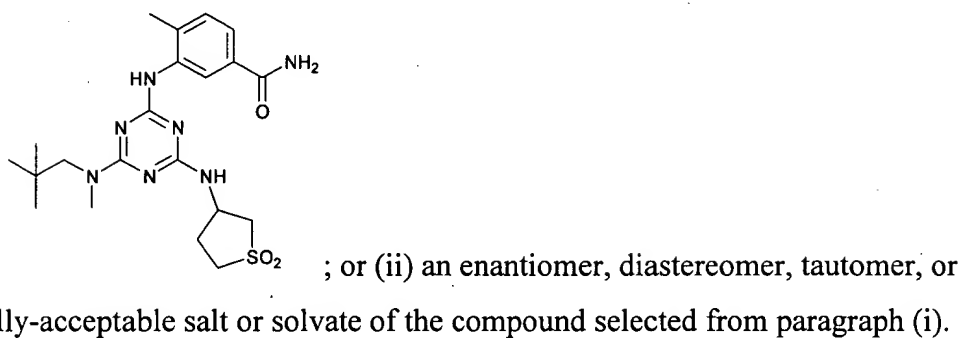
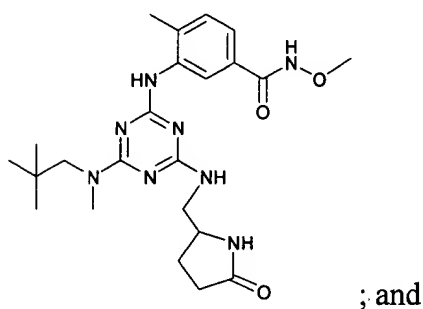
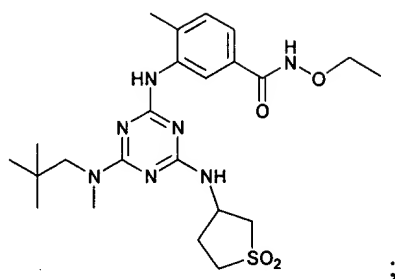
76 (Previously presented). A compound of Claim 70 or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt or solvate thereof wherein:

$R^9$  is chosen from substituted or unsubstituted 1,2,4-triazole; substituted or unsubstituted thiazole connected via a C2, C4, or C5 position; substituted or unsubstituted 1,3,4-oxdiazole connected via a 2 or 5 position; and substituted or unsubstituted imidazole connected via a C2, C4, C5, N1 or N3 position.

77 (Previously presented). A compound which is selected from (i):



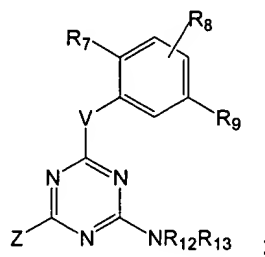




78 (Previously presented). A pharmaceutical composition comprising as an active ingredient, a compound, or a salt thereof, according to claim 70, and a pharmaceutically acceptable carrier.



79 (Amended). A pharmaceutical composition ~~according to claim 78, comprising as an~~  
active ingredient, a compound having the formula,



or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt or solvate  
thereof, wherein:

V is chosen from  $-\text{CHR}^5-$ ,  $-\text{NR}^5-$ ,  $-\text{O}-$ , and  $-\text{S}-$ ;

Z is halogen, alkyl,  $-N(R^1)(R^2)$ , or alkyl substituted with one to two of  $-N(R^{31})(R^{32})$ , alkoxy, alkylthio, halogen, cyano, carboxyl, hydroxyl,  $-SO_2$ -alkyl,  $-CO_2$ -alkyl,  $-C(O)$ -alkyl, nitro, cycloalkyl, substituted cycloalkyl,  $-C(O)-N(R^{31})(R^{32})$ , and/or  $-NH-C(O)$ -alkyl;

$R^1$  is hydrogen or methyl;

R<sup>2</sup> is alkyl of 1 to 8 carbon atoms;

- R<sup>3</sup> is chosen from hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R<sup>5</sup> is chosen from hydrogen and alkyl of 1 to 4 carbon atoms;

R<sup>7</sup> is chosen from hydrogen, amino, aminoC<sub>1-4</sub>alkyl, halogen, cyano, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy,  
and alkylthio;

R<sup>8</sup> is attached to any available carbon atom of the phenyl ring and is chosen from hydrogen and halogen;

R<sup>9</sup> is chosen from -C(O)N(R<sup>31</sup>)(R<sup>32</sup>), -SO<sub>2</sub>N(R<sup>31</sup>)(R<sup>32</sup>), -N(R<sup>33</sup>)SO<sub>2</sub>R<sup>34</sup>, -C(O)N(R<sup>33</sup>)N(R<sup>31</sup>)(R<sup>32</sup>), -N(R<sup>33</sup>)C(O)R<sup>34</sup>, -CH<sub>2</sub>N(R<sup>33</sup>)C(O)R<sup>34</sup>, -N(R<sup>31</sup>)(R<sup>32</sup>), -CH<sub>2</sub>OC(O)R<sup>34</sup>, heterocyclyl, and substituted heterocyclyl; or

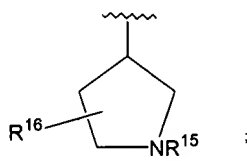
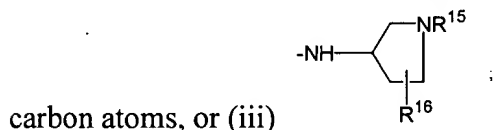
$R^8$  and  $R^9$  taken together may form  $-C(O)N(R^{33})CH_2-$  or  $-C(O)N(R^{33})C(O)-$ ;

R<sup>31</sup> and R<sup>33</sup> are independently chosen from hydrogen, alkyl, and substituted alkyl;

R<sup>32</sup> is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, aryloxy, heterocyclyl and substituted heterocyclyl;

R<sup>34</sup> is chosen from alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

-N(R<sup>12</sup>)(R<sup>13</sup>) taken together form (i) a monocyclic heterocyclyl or substituted heterocyclyl of 5 to 7 atoms having 1, 2 or 3 additional nitrogen atoms, (ii) -NH-alkyl wherein alkyl is of 1 to 4

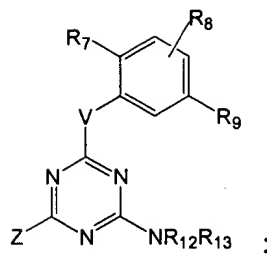


R<sup>15</sup> and R<sup>16</sup> are independently hydrogen or methyl; and  
R<sup>17</sup> is chosen from hydrogen, alkyl, substituted alkyl, -C(O)-alkyl,  
-C(O)-substituted alkyl, -C(O)-aryl, and -C(O)-substituted aryl and further comprising one or more  
additional active ingredients.

80 (Previously presented). A pharmaceutical composition according to claim 79, wherein said additional active ingredient is an anti-inflammatory compound or an immunosuppressive agent.

81 (Previously presented). A pharmaceutical composition according to claim 79, wherein said additional active ingredient is chosen from a steroid and an NSAID.

82 (Amended). A method of treating rheumatoid arthritis, the method comprising administering to a mammal an effective amount of a composition ~~according to claim 78~~ comprising as an active ingredient, a compound having the formula,



or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt or solvate thereof, wherein:

V is chosen from  $-\text{CHR}^5-$ ,  $-\text{NR}^5-$ ,  $-\text{O}-$ , and  $-\text{S}-$ ;

Z is halogen, alkyl,  $-\text{N}(\text{R}^1)(\text{R}^2)$ , or alkyl substituted with one to two of  $-\text{N}(\text{R}^{31})(\text{R}^{32})$ , alkoxy, alkylthio, halogen, cyano, carboxyl, hydroxyl,  $-\text{SO}_2$ -alkyl,  $-\text{CO}_2$ -alkyl,  $-\text{C}(\text{O})$ -alkyl, nitro, cycloalkyl, substituted cycloalkyl,  $-\text{C}(\text{O})-\text{N}(\text{R}^{31})(\text{R}^{32})$ , and/or  $-\text{NH}-\text{C}(\text{O})$ -alkyl;

$\text{R}^1$  is hydrogen or methyl;

$\text{R}^2$  is alkyl of 1 to 8 carbon atoms;

$\text{R}^3$  is chosen from hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

$\text{R}^5$  is chosen from hydrogen and alkyl of 1 to 4 carbon atoms;

$\text{R}^7$  is chosen from hydrogen, amino, amino $\text{C}_{1-4}$ alkyl, halogen, cyano,  $\text{C}_{1-4}$ alkyl,  $\text{C}_{1-4}$ alkoxy, and alkylthio;

$\text{R}^8$  is attached to any available carbon atom of the phenyl ring and is chosen from hydrogen and halogen;

$\text{R}^9$  is chosen from  $-\text{C}(\text{O})\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{SO}_2\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{N}(\text{R}^{33})\text{SO}_2\text{R}^{34}$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{33})\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{N}(\text{R}^{33})\text{C}(\text{O})\text{R}^{34}$ ,  $-\text{CH}_2\text{N}(\text{R}^{33})\text{C}(\text{O})\text{R}^{34}$ ,  $-\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{CH}_2\text{OC}(\text{O})\text{R}^{34}$ , heterocyclyl, and substituted heterocyclyl; or

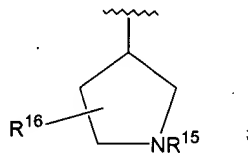
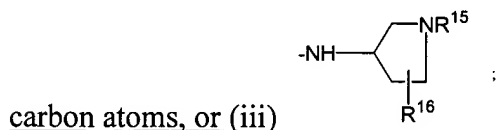
$\text{R}^8$  and  $\text{R}^9$  taken together may form  $-\text{C}(\text{O})\text{N}(\text{R}^{33})\text{CH}_2-$  or  $-\text{C}(\text{O})\text{N}(\text{R}^{33})\text{C}(\text{O})-$ ;

$\text{R}^{31}$  and  $\text{R}^{33}$  are independently chosen from hydrogen, alkyl, and substituted alkyl;

$\text{R}^{32}$  is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, aryloxy, heterocyclyl and substituted heterocyclyl;

$\text{R}^{34}$  is chosen from alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

-N(R<sup>12</sup>)(R<sup>13</sup>) taken together form (i) a monocyclic heterocyclyl or substituted heterocyclyl of 5 to 7 atoms having 1, 2 or 3 additional nitrogen atoms, (ii) -NH-alkyl wherein alkyl is of 1 to 4



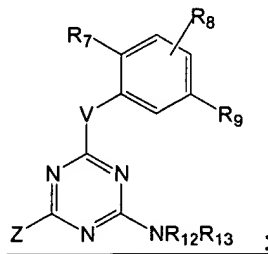
R<sup>15</sup> and R<sup>16</sup> are independently hydrogen or methyl; and  
R<sup>17</sup> is chosen from hydrogen, alkyl, substituted alkyl, -C(O)-alkyl,  
-C(O)-substituted alkyl, -C(O)-aryl, and -C(O)-substituted aryl.

83-84 (Canceled).

85 (Amended). The method according to claim 82 wherein said composition ~~according to claim 78~~ is administered with one or more additional anti-inflammatory or immunosuppressive agents as a single dose form or as separate dosage forms.

86-87 (Canceled).

88 (Amended). A method of inhibiting TNF- $\alpha$  expression in a mammal, the method comprising administering to the mammal an effective amount of a composition ~~according to claim 78~~ comprising as an active ingredient, a compound having the formula,



or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt, or solvate thereof, wherein:

V is chosen from  $-\text{CHR}^5-$ ,  $-\text{NR}^5-$ ,  $-\text{O}-$ , and  $-\text{S}-$ ;

Z is halogen, alkyl,  $-\text{N}(\text{R}^1)(\text{R}^2)$ , or alkyl substituted with one to two of  $-\text{N}(\text{R}^{31})(\text{R}^{32})$ , alkoxy, alkylthio, halogen, cyano, carboxyl, hydroxyl,  $-\text{SO}_2$ -alkyl,  $-\text{CO}_2$ -alkyl,  $-\text{C}(\text{O})$ -alkyl, nitro, cycloalkyl, substituted cycloalkyl,  $-\text{C}(\text{O})-\text{N}(\text{R}^{31})(\text{R}^{32})$ , and/or  $-\text{NH}-\text{C}(\text{O})$ -alkyl;

$\text{R}^1$  is hydrogen or methyl;

$\text{R}^2$  is alkyl of 1 to 8 carbon atoms;

$\text{R}^3$  is chosen from hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

$\text{R}^5$  is chosen from hydrogen and alkyl of 1 to 4 carbon atoms;

$\text{R}^7$  is chosen from hydrogen, amino, amino $\text{C}_{1-4}$ alkyl, halogen, cyano,  $\text{C}_{1-4}$ alkyl,  $\text{C}_{1-4}$ alkoxy, and alkylthio;

$\text{R}^8$  is attached to any available carbon atom of the phenyl ring and is chosen from hydrogen and halogen;

$\text{R}^9$  is chosen from  $-\text{C}(\text{O})\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{SO}_2\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{N}(\text{R}^{33})\text{SO}_2\text{R}^{34}$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{33})\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{N}(\text{R}^{33})\text{C}(\text{O})\text{R}^{34}$ ,  $-\text{CH}_2\text{N}(\text{R}^{33})\text{C}(\text{O})\text{R}^{34}$ ,  $-\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{CH}_2\text{OC}(\text{O})\text{R}^{34}$ , heterocyclyl, and substituted heterocyclyl; or

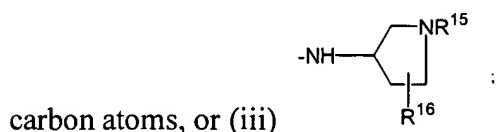
$\text{R}^8$  and  $\text{R}^9$  taken together may form  $-\text{C}(\text{O})\text{N}(\text{R}^{33})\text{CH}_2-$  or  $-\text{C}(\text{O})\text{N}(\text{R}^{33})\text{C}(\text{O})-$ ;

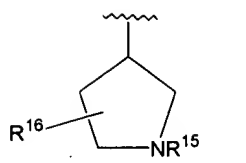
$\text{R}^{31}$  and  $\text{R}^{33}$  are independently chosen from hydrogen, alkyl, and substituted alkyl;

$\text{R}^{32}$  is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, aryloxy, heterocyclyl and substituted heterocyclyl;

$\text{R}^{34}$  is chosen from alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

$-\text{N}(\text{R}^{12})(\text{R}^{13})$  taken together form (i) a monocyclic heterocyclyl or substituted heterocyclyl of 5 to 7 atoms having 1, 2 or 3 additional nitrogen atoms, (ii)  $-\text{NH}$ -alkyl wherein alkyl is of 1 to 4

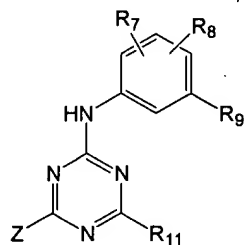




R<sup>15</sup> and R<sup>16</sup> are independently hydrogen or methyl; and  
R<sup>17</sup> is chosen from hydrogen, alkyl, substituted alkyl, -C(O)-alkyl,  
-C(O)-substituted alkyl, -C(O)-aryl, and -C(O)-substituted aryl.

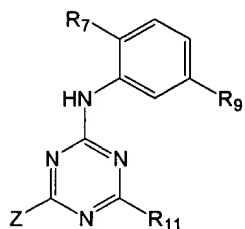
89-95 (Canceled).

96 (Previously presented). A compound according to claim 66, having the formula,



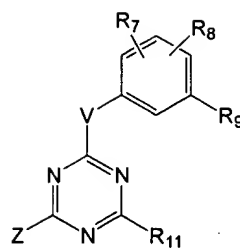
, or pharmaceutically-acceptable salt or solvate thereof.

97 (Previously presented). A compound according to claim 66, having the formula,



or pharmaceutically-acceptable salt or solvate thereof.

98 (Amended). A compound ~~according to claim 66,~~ having the formula,



**I**

or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt, or solvate thereof, wherein:

V is chosen from  $-\text{CHR}^5$ -,  $-\text{NR}^5$ -,  $-\text{O}$ -, and  $-\text{S}$ -;

Z is chosen from halogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl,  $-\text{SR}^3$ ,  $-\text{OR}^3$ , and  $-\text{N}(\text{R}^1)(\text{R}^2)$ ;  $-\text{N}(\text{R}^1)(\text{R}^2)$  taken together may form a heterocyclyl or substituted heterocyclyl; or

$\text{R}^1$  is chosen from hydrogen, alkyl and substituted alkyl; and

$\text{R}^2$  is chosen from alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

$\text{R}^3$  is chosen from hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

$\text{R}^5$  is chosen from hydrogen and alkyl, or when attached to a nitrogen atom,  $\text{R}^5$  taken together with  $\text{R}^7$  may form a fused heterocyclyl or substituted heterocyclyl;

$\text{R}^7$  is chosen from hydrogen,  $-\text{N}(\text{R}^{31})(\text{R}^{32})$ , halogen, cyano, alkyl, substituted alkyl, alkoxy, and alkylthio, or when V is  $-\text{NR}^5$ ,  $-\text{R}^5$  and  $\text{R}^7$  taken together may form a fused heterocyclyl or substituted heterocyclyl;

$\text{R}^8$  is chosen from hydrogen and halogen;

$\text{R}^9$  is chosen from  $-\text{CO}_2(\text{alkyl})$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{SO}_2\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{N}(\text{R}^{33})\text{SO}_2\text{R}^{34}$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{33})\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{N}(\text{R}^{33})\text{C}(\text{O})\text{R}^{34}$ ,  $-\text{CH}_2\text{N}(\text{R}^{33})\text{C}(\text{O})\text{R}^{34}$ ,  $-\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{CH}_2\text{OC}(\text{O})\text{R}^{34}$ ,  $\text{C}_{1-6}\text{alkyl}$ , substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclyl, substituted heterocyclyl, and  $-\text{C}(\text{O})\text{R}^{10}$ ; provided, however, that when  $\text{R}^9$  is  $\text{CH}_3$  or  $\text{NH}_2$ , then neither  $\text{R}^2$  nor  $\text{R}^{14}$  is *para*-cyano-phenyl;

or  $\text{R}^8$  and  $\text{R}^9$  taken together may form  $-\text{C}(\text{O})\text{N}(\text{R}^{33})\text{CH}_2$ - or  $-\text{C}(\text{O})\text{N}(\text{R}^{33})\text{C}(\text{O})$ -;

$\text{R}^{10}$  is chosen from heterocyclyl, substituted heterocyclyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkyl, and substituted alkyl;

R<sup>31</sup> and R<sup>33</sup> are independently chosen from hydrogen, alkyl, and substituted alkyl;

R<sup>32</sup> is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, aryloxy, heterocyclyl and substituted heterocyclyl;

R<sup>34</sup> is chosen from alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

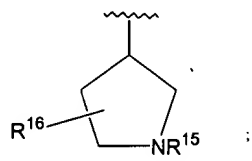
R<sup>12</sup> is chosen from hydrogen, alkyl, and substituted alkyl; and

R<sup>13</sup> is -(CH<sub>2</sub>)<sub>m</sub>R<sup>14</sup>; or

-N(R<sup>12</sup>)(R<sup>13</sup>) taken together may form a heterocyclyl or substituted heterocyclyl;

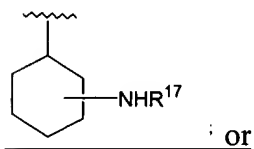
m is 0, 1, 2 or 3;

R<sup>14</sup> is chosen from alkyl, substituted alkyl, -C(O)N(R<sup>31</sup>)(R<sup>32</sup>), -N(R<sup>33</sup>)C(O)R<sup>34</sup>, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, and



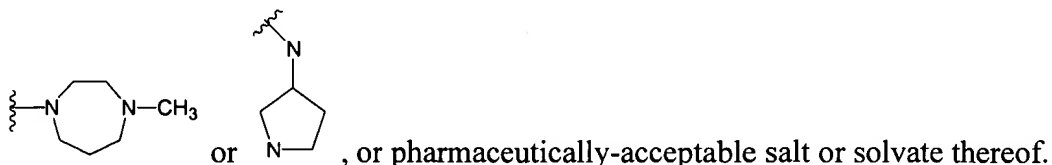
R<sup>15</sup> is chosen from hydrogen, alkyl, substituted alkyl, alkenyl, -C(O)-alkyl, -C(O)-substituted alkyl, -C(O)-aryl, -C(O)-substituted aryl, -C(O)-alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

R<sup>16</sup> is chosen hydrogen, alkyl, substituted alkyl, and



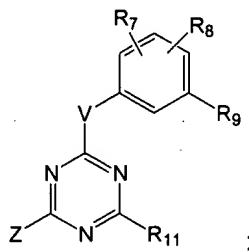
R<sup>17</sup> is chosen from hydrogen, alkyl, substituted alkyl, -C(O)-alkyl, -C(O)-substituted alkyl, -C(O)-aryl, and -C(O)-substituted aryl;

and wherein R<sub>11</sub> is





99 (Previously presented). A method of modulating p38 kinase in a mammal comprising administering to the mammal at least one compound having the formula,



or an enantiomer, diastereomer, tautomer, or pharmaceutically-acceptable salt, or solvate thereof, wherein:

V is chosen from  $-\text{CHR}^5$ -,  $-\text{NR}^5$ -,  $-\text{O}$ -, and  $-\text{S}$ -;

Z is chosen from halogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl,  $-\text{SR}^3$ ,  $-\text{OR}^3$ , and  $-\text{N}(\text{R}^1)(\text{R}^2)$ ;

$-\text{N}(\text{R}^1)(\text{R}^2)$  taken together may form a heterocyclyl or substituted heterocyclyl; or

$\text{R}^1$  is chosen from hydrogen, alkyl and substituted alkyl; and

$\text{R}^2$  is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

$\text{R}^3$  is chosen from hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

$\text{R}^5$  is chosen from hydrogen and alkyl, or when attached to a nitrogen atom,  $\text{R}^5$  taken together with  $\text{R}^7$  may form a fused heterocyclyl or substituted heterocyclyl;

$\text{R}^7$  is chosen from hydrogen,  $-\text{N}(\text{R}^{31})(\text{R}^{32})$ , halogen, cyano, alkyl, substituted alkyl, alkoxy, and alkylthio, or when V is  $-\text{NR}^5$ ,  $-\text{R}^5$  and  $\text{R}^7$  taken together may form a fused heterocyclyl or substituted heterocyclyl;

$\text{R}^8$  is chosen from hydrogen and halogen;

$\text{R}^9$  is chosen from  $-\text{CO}_2(\text{alkyl})$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{SO}_2\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{N}(\text{R}^{33})\text{SO}_2\text{R}^{34}$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{33})\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{N}(\text{R}^{33})\text{C}(\text{O})\text{R}^{34}$ ,  $-\text{CH}_2\text{N}(\text{R}^{33})\text{C}(\text{O})\text{R}^{34}$ ,  $-\text{N}(\text{R}^{31})(\text{R}^{32})$ ,  $-\text{CH}_2\text{OC}(\text{O})\text{R}^{34}$ ,  $\text{C}_{1-6}\text{alkyl}$ , substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclyl, substituted heterocyclyl, and  $-\text{C}(\text{O})\text{R}^{10}$ ; provided, however, that when  $\text{R}^9$  is  $\text{CH}_3$  or  $\text{NH}_2$ , then neither  $\text{R}^2$  nor  $\text{R}^{14}$  is *para*-cyano-phenyl;

or  $R^8$  and  $R^9$  taken together may form  $-C(O)N(R^{33})CH_2-$  or  $-C(O)N(R^{33})C(O)-$ ;

$R^{10}$  is chosen from heterocyclyl, substituted heterocyclyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, alkyl, and substituted alkyl;

$R^{31}$  and  $R^{33}$  are independently chosen from hydrogen, alkyl, and substituted alkyl;

$R^{32}$  is chosen from hydrogen, alkyl, substituted alkyl, alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, aryloxy, heterocyclyl and substituted heterocyclyl;

$R^{34}$  is chosen from alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

$R^{11}$  is  $-N(R^{12})(R^{13})$ ;

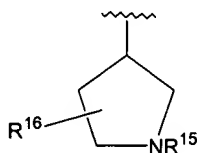
$R^{12}$  is chosen from hydrogen, alkyl, and substituted alkyl;

$R^{13}$  is  $-(CH_2)_mR^{14}$ ;

$-N(R^{12})(R^{13})$  taken together may form a heterocyclyl or substituted heterocyclyl;

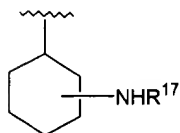
$m$  is 0, 1, 2 or 3;

$R^{14}$  is chosen from hydrogen, alkyl, substituted alkyl,  $-C(O)N(R^{31})(R^{32})$ ,  $-N(R^{33})C(O)R^{34}$ , aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl, substituted heterocyclyl, and



$R^{15}$  is chosen from hydrogen, alkyl, substituted alkyl, alkenyl,  $-C(O)$ -alkyl,  $-C(O)$ -substituted alkyl,  $-C(O)$ -aryl,  $-C(O)$ -substituted aryl,  $-C(O)$ -alkoxy, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclyl and substituted heterocyclyl;

$R^{16}$  is chosen hydrogen, alkyl, substituted alkyl, and



or

$R^{17}$  is chosen from hydrogen, alkyl, substituted alkyl,  $-C(O)$ -alkyl,  $-C(O)$ -substituted alkyl,  $-C(O)$ -aryl, and  $-C(O)$ -substituted aryl.